

REMARKS

I. Status of the claims

Claims 12–21 and 23–33 are cancelled herein.

Claims 1 and 3–6 are amended and new claims 34–37 are added.

Claims 1, 3–8, and 34–37 are currently pending.

II. Restriction Requirement

As required in section “5.” of the Office Action, Applicant hereby affirms the election of the group I claims with respect to codons 82/84; with elected probes SEQ ID NO:267 and SEQ ID NO:354 and primer pair SEQ ID NO:3 and SEQ ID NO:4, as previously made during the 1/28/03 telephone conversation between the Examiner and Ms. Patricia A. Kammerer.

III. Objections to the Claims

Claim 31 is objected for impermissibly referring to Figure 1. In response to this objection, Applicant notes that claim 31 is cancelled by the current amendment. Objection to this claims is therefore moot and should be withdrawn.

IV. Objections to the Specification

A. The disclosure is objected to because the tables are not numbered sequentially. In response, Applicant has amended the Specification so that the tables now appear in numeric sequence as required.

B. The disclosure is further objected because the “specification and figures recite nucleotide sequences that are not properly identified by sequence identifiers” In response Applicant has amended the Specification so that all sequences are properly identified and are part of a Sequence Listing in accordance with 37 C.F.R. § 1.821–§1.825. Furthermore, a substitute sequence, with the required request to amend the Specification, and the required Sequence Listing Statement are also enclosed.

In view of the described amendments to the Specification and the submission of the substitute Sequence Listing (and required statement), Applicant believes that this objection has been overcome and may now properly be withdrawn.

V. Rejection under 35 U.S.C. §112

Claims 1, 3–6, 30, and 31 are rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. Applicant respectfully traverses.

A. Claim 1 (and claims depending therefrom) are alleged to be indefinite because both steps “a)” and “b)” are:

recited as being optional (*i.e.* performed ‘if need be’), yet step (c) requires the nucleic acid of step (a) or (b) for hybridization with the recited at least two probes, thus, step c(c) implies that at least one of steps (a) or (b) must be carried out, but steps (a) and (b) are not consistent with this implication. Thus the claim is unclear as to which steps are required.

In response applicant notes that, as currently amended, neither step “a)” nor “b)” is optional in claim 1. Moreover, claim 3, as amended, recites that only step “b)” is optional. Applicant believes that this amendment overcomes this rejection of claims 1 and 3 and all claims depending therefrom.

B. Claim 1, step (a) is rejected as allegedly being indefinite because “the phrase ‘the polynucleic acids’ lacks proper antecedent basis. As currently amended the claim now recites “a biological sample comprising polynucleic acids”, thereby providing the required antecedent basis. Applicant believes that this amendment overcomes the Examiner’s rejection.

C. Claim 1, is rejected as allegedly lacking antecedent basis for the use of the phrase “the relevant part of the protease gene” in step (b). In response, claim 1 has been amended to recite “amplifying part of a protease gene of HIV comprising codons 82 and 84”. Applicant believes that this amendment overcomes the Examiner’s rejection.

D. Claim 1 and the claims depending therefrom are rejected as allegedly being indefinite for their use of the phrase “codon 82/84”. The Examiner states that:

it is not clear if this means that the probes must hybridize to codon 82 and 84 or if this means that the probes must hybridize to codon 82 or codon 84. It is not clear if the use of a probe that hybridizes to one but not the other is encompassed within the scope of the instant claims.

Applicant respectfully directs the Examiner’s attention to the Specification which recites that one of the aims of the present invention is to provide “probes specifically hybridizing to a target sequence comprising codon 82 and/or 84” (*see*, for example, page 5, line 2 of the specification). From this, Applicant believes that it is clear that the claim is drawn to probes which hybridize to either codon 82 or 84 or to both 82 and 84. Applicant believes that this explanation provides the required clarification and thereby overcomes the Examiner’s rejection. Nevertheless, as currently amended the claims no longer recite the rejected phrase “codon 82/84”. Consequently, this rejection is now moot and should be withdrawn.

E. The Examiner further asserts that “[i]n claim 1, part (d), ‘said target sequences’ lacks proper antecedent basis because the claim previously refers to singular target sequence....” In response Applicant notes that claim 1 as currently amended recites “target sequence” in part “d)”. It is believed that this amendment overcomes the Examiner’s rejection.

F. Claims 5 and 6 are rejected as allegedly being indefinite for reciting that:

step (b) comprises amplifying a fragment, but it is not clear if this step (b) recited in claims 5 and 6 is meant to replace the step (b) in claim 1 or is meant to merely define the amplifying that is to take place ‘if need be.’ That is, it is not clear if the amplification recited in claims 5 and 6 is required to take place in the method or if the amplification recited in claims 5 and 6 is to take place ‘if need be’ as is recited in the independent claim.

Applicant respectfully traverses.

As currently amended, claims 5 and 6 now depend from claim 3. Moreover, claims 5 and 6 now recite the specific action required to be performed as step b). That is, claims 5 and 6 recite step b) as a required, not an optional, step.

G. Claims 5 and 6 are further rejected as allegedly being indefinite for the

recitation of specific nucleotide positions in the protease gene, for example, the recitation ‘located at nucleotide position 210–260 of the protease gene’ because such positions are entirely arbitrary when they are recited without particular reference to a recitation of the protease gene. The nucleotide positions in a recitation of the gene are entirely context dependent on a given disclosure of the gene, whether the disclosure provides 5’ untranslated regions, includes introns, is within the context of the entire HIV genome, etc. It is not known from the recitations in the claims what the context for the numbering used in the claims is, and thus the metes and bounds of the required primers is unclear.

Applicant respectfully traverses.

As currently amended claims 5 and 6 now recite that the nucleotide numbering refers to the “coding portion of the protease gene”. Applicant asserts that this provides the “frame of reference” require to render claims 5 and 6 definite. Accordingly, Applicant believes that this rejection of the claims has been overcome and should be withdrawn.

H. Claim 31 is rejected as allegedly being indefinite for its recitation “wherein the target sequence for codon 82/84 are shown in Figure 1. . . .” In response, Applicant points out that claim 31 is cancelled by the above amendment to the claims. Consequently, this rejection is moot and should be withdrawn.

I. In view of the Amendments to the claims and the foregoing arguments, Applicant believes that all rejections under 35 U.S.C. §112 have been overcome and may properly be withdrawn.

VI. Rejection under 35 U.S.C. §102

Claim 1 is rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Kozal *et al.* (Nature Medicine, 1996, 2:753-759). Specifically, the Examiner asserts that

Kozal *et al.* teach a method in which amplified portions of the HIV protease gene are sequenced by hybridization to a solid support (referred to as a chip), wherein a set of four 15-base oligonucleotide probes differing in the 7 nucleotide position is used to determine the identity of each base in the protease gene (Fig. 3 and p. 758). Using this methodology, Kozal *et al.* detected the presence of mutations at codon 82 of the protease gene that confers resistance to antiviral drugs (see Figure 1).

Applicant respectfully traverses.

As set out in *MPEP* chapter 2100:

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.’ *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).” *MPEP* §2131.

As currently amended, claim 1 now recites that the hybridization step must take place using “probes having the sequence of SEQ ID NO:267 and SEQ ID NO:354, or probes having sequence complementary to SEQ ID NO:267 or SEQ ID NO:354”. There is nothing in the Kozal *et al.* reference which describes the use of these specific probes. As stated by the Examiner a method “which utilizes a pair of probes consisting of SEQ ID NO:267 and SEQ ID NO: 354” is “free of the prior art” (*see* page 12 of the Office Action). Accordingly, Applicant believes that this rejection of claim 1 under 35 U.S.C. §102(b) has been overcome and may properly be withdrawn.

VII. Rejection under 35 U.S.C. §103

Claims 1, 3, 5, 6, and 31 are rejected as allegedly being unpatentable over Stuyver *et al.* (WO 97/27332) in view of Eastman *et al.* (Journal of Virology, 72:5154-5164, June, 1998).

Specifically, the Examiner alleges that:

it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used probes taught by Eastman *et al.* in the methods taught by Stuyver *et al.* The ordinary practitioner would have been motivated to look to the teachings of Eastman *et al.* for probes to codon 82/84 of the HIV protease gene because Stuyver *et al.* specifically teach that their method

could easily be extended to include protease codons associated with antiviral drug resistance, and Eastman *et al.* teach hybridization probes that have been successfully used to probe such mutations in codons 82/84 of the HIV protease gene, thus, in light of the teachings of Stuyver *et al.* in view of Eastman *et al.*, the instant invention is *prima facie* obvious in view of the prior art.

Applicant respectfully traverses.

MPEP 706.02(j) provides the following criteria which must be met in order to establish obviousness.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added).

Applicant asserts that all of the requirements necessary to establish a *prima facie* case of obviousness for the instantly pending claims, as set out in MPEP 706.02(j) are not met by the combination of the cited references. Applicant asserts that the combination of Stuyver *et al.* and Eastman *et al.* do not teach or suggest the use of the use of probes having the sequence of SEQ ID NO:267 and 354 or their complements. As the Examiner noted, a method utilizing probes having the sequence of SEQ ID NO:267 and 354 is free from the prior art. Applicant assert that the same is true for a method utilizing probes having the sequence of the complement of SEQ ID NO:267 and 354.

The combination of the cited art neither teaches nor suggests the desirability of such a method. Accordingly, Applicant asserts that the combination of the cited art fails to meet the elements set out in MPEP §706.02(j) as being required to establish a *prima facie* case of obviousness. Specifically, the combination of the cited references provides no teaching or

suggestion that would motivate the artisan of ordinary skill to modify the cited art so as to achieve the claimed invention; the combination of the cited art does not teach all of the current claim limitations; and the combination of the cited art provides no reasonable expectation that the currently claimed invention would be successful for detecting mutant HIV.

In view of the amendments to the claims and the foregoing arguments, Applicant contends that the rejection of the pending claims under 35 U.S.C. § 103(a) has been overcome and may now properly be withdrawn.

VIII. Conclusions

In view of the foregoing Amendments and Remarks, Applicant believes that all outstanding objections to the claims and Specification and rejections of the claims have been overcome. Accordingly, it is believed that the case is now in condition for immediate allowance. Consequently, Applicant respectfully requests favorable reconsideration of this case and issuance of a "Notice of Allowance" therefor.

The Examiner is invited to contact the undersigned patent agent at (713) 787-1589 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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